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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/836,012	04/17/2001	Jeffrey R. Sampson	10992153-1 (2003309-0013)	6991
22878	7590	08/23/2005	EXAMINER CHUNDURU, SURYAPRABHA	
AGILENT TECHNOLOGIES, INC. INTELLECTUAL PROPERTY ADMINISTRATION, LEGAL DEPT. P.O. BOX 7599 M/S DL429 LOVELAND, CO 80537-0599			ART UNIT 1637	PAPER NUMBER

DATE MAILED: 08/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/836,012

Applicant(s)

SAMPSON ET AL.

Examiner

Suryaprabha Chunduru

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-17 and 74-83 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-17 and 74-83 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

**DETAILED ACTION**

1. Applicants' response to the office action filed on June 14, 2005 has been entered.

***Status of the Application***

2. Claims 1-17, 74-83 are pending. Claims 1, 1-2, 7, 12, 14, and 81-83 are amended. All amendments and arguments have been thoroughly reviewed and deemed persuasive in view of amendment. The rejections made in the previous office action that are not reiterated herein are withdrawn in view of the amendment. This action is made Final, necessitated by Amendment.

***New Grounds of Rejections necessitated by amendment***

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 1-17, 74-83 rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al. (WO 95/04160) in view of Sorge (USPN. 6,607,878).

Southern et al. teach a composition (mixture) of claims 1-2, 7, 12, 14, 81-82, comprising X-mer precursor having a minimum length of 6 nucleotides (see page 5, line 28-36, page 55, line 13-23, page 2, line 27-33), wherein the mixture the mixture has at least complexity of at least  $56/N$ , wherein N represents the number of distinct X-mers (see page 5, line 28-36, Fig. 3a, page 55, line 13-23); wherein the mixture comprises a set of tags (reporter groups) and each tag is covalently linked to at least one X-mer through a cleavable linkage (see page 6, paragraph 2, page 7, line 3-6, page 14, line 1-24).

With regard to claims 2, Southern et al. also teach that X-mer precursors comprise isotopic composition (see page 7, line 3-12);

With regard to claims to claims 3-6, Southern et al. teach 4096 different hexanucleotides with known oligonucleotide sequences (which includes sets of X-mers ranging from 128 to 512) (see page 5, line 28-30, page 42, line 1-30);

With regard to claim 7, Southern et al. teach that the number tags distinguishable by mass spectrometry includes 20- 4096 (each X-mer having a unique tag) (see page 5, line 28-30, page 2, lines 27-33);

With regard to claims 8-11, Southern et al. teach that 4096 number of unique tags (which includes the number ranging from 10-5000) (see page 5, line 28-30);

With regard to claim 12-17, 83, Southern et al. teach that said number of tags is greater than a mass complexity of a natural equivalent (without a tag) and the increment in adding a reporter is larger than the mass difference between the smallest and the largest tag (page 7, line 27-35, page 8, table 2, that indicates 0.5%-100% number of tags).

With regard to claim 6, Brenner teaches that the nucleotide sequences of the precursors of said mixture are known (see col. 7, table II).

However Southern et al. did not specifically teach any oligonucleotide sequence in the mixture is attached to preferably a single tag with a discrete molecular weight, tags distinguishable by mass spectrometry and kit comprising said mixture of X-mer precursors.

Sorge et al. teach collection of uniquely tagged molecules wherein Sorge teach the use of oligonucleotide tags, each with discrete molecular weight (see col. 22, line 56-67, col. 23, line 1-6). Sorge also teaches that the use of molecular weight tags would allow for unambiguous identification of molecular weight after cleavage and provide sequence information of each DNA fragment in a given restriction pattern and identification of any particular nucleotide sequence in the mixture (see col. 23, line 1-22). Sorge also teaches tags that are distinguishable by mass spectrometry and a kit comprising said mixture of DNA fragments (see col. 27, line 10-67).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the mixture of x-mer precursors as taught by Southern et al. with a step of using tags with discrete molecular weight as taught by Sorge for the purpose of enriching tagged precursors by targeting size differences in oligonucleotide tags to provide an efficient sorting of DNA fragments in a mixture. One skilled in the art would be motivated to combine the mixture of x-mers as taught by Southern et al. with the inclusion molecular weight tags as taught by as taught by Sorge because Sorge explicitly taught that the use of molecular weight tags would allow for unambiguous identification of molecular weight after cleavage and provide sequence information of each DNA fragment in a given restriction pattern and identification of any particular nucleotide sequence in the mixture (see col. 23, line 1-22). Sorge

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also explicitly taught tags that are distinguishable by mass spectrometry and a kit comprising said mixture of DNA fragments (see col. 27, line 10-67). An ordinary artisan would have a reasonable expectation of success that inclusion of discrete molecular weight tags would result in enriching sequence information of any oligonucleotide of interest in the mixture, further incorporating tags that are distinguishable by mass spectrometry would enhance the sensitivity of the detectable mass tags and improve the identification of sequence information. And packaging the collection tagged molecules in a kit format would result in a cost-effective and ready to use x-mer precursors for various molecular analysis and such modification of the X-mer mixture would be obvious over the cited prior art in the absence of secondary considerations.

B. Claims 1, 3-6, 74-80 are rejected 35 U.S.C. 103(a) as being unpatentable over Brenner (USPN. 5,654,413) in view of Sorge (6,607,878).

Brenner teaches a composition (mixture) of claims 1, 3-5, comprising X-mer precursor having a minimum length of 3 nucleotides (see col. 3, line 15-67, col. 4, line 1-8, col. 7, line 39-60), wherein the mixture the mixture has at least complexity of at least  $56/N$ , wherein  $N$  represents the number of distinct X-mers (see col. 7, table II shows complexity of at least  $56/N$ ); wherein the mixture comprises a set of tags and each tag is covalently linked to at least one X-mer through a cleavable linkage (see col. 9, line 25-67, col. 10, line 1-67, col. 11, line 1-65).

With regard to claim 6, Brenner teaches that the nucleotide sequences of the precursors of said mixture are known (see col. 7, table II);

With regard to claims 74-80, Brenner teaches a kit composition comprising said mixture of x-mer precursors (comprising natural or non-natural nucleotides, see col. 5, line 37-44), enzymes such as polymerases (polymerases are also considered as condensing agent herein,

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since the instant specification did not define the term condensing agent nor given any specific examples of a condensing agent), ligases, an array comprising surface and multiplicity of sequence probes (oligonucleotides) attached to it (see col. 23, line 40-57, col. 17, line 35-63, col. 18, line 43-67).

However Brenner did not specifically teach any oligonucleotide sequence in the mixture is attached to preferably a single tag with a discrete molecular weight, tags distinguishable by mass spectrometry

Sorge et al. teach collection of uniquely tagged molecules wherein Sorge teach the use of oligonucleotide tags, each with discrete molecular weight (see col. 22, line 56-67, col. 23, line 1-6). Sorge also teaches that the use of molecular weight tags would allow for unambiguous identification of molecular weight after cleavage and provide sequence information of each DNA fragment in a given restriction pattern and identification of any particular nucleotide sequence in the mixture (see col. 23, line 1-22). Sorge also teaches tags that are distinguishable by mass spectrometry and a kit comprising said mixture of DNA fragments (see col. 27, line 10-67).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the mixture of x-mer precursors as taught by Brenner with a step of using tags with discrete molecular weight that are distinguishable by mass spectrometry as taught by Sorge for the purpose of enriching tagged precursors by targeting size differences in oligonucleotide tags to provide an efficient and sensitive sorting of DNA fragments in a mixture. One skilled in the art would be motivated to combine the mixture of x-mers as taught by Brenner with the inclusion molecular weight tags as taught by Sorge because Sorge explicitly taught that the use of molecular weight tags would allow for unambiguous identification of molecular

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weight after cleavage and provide sequence information of each DNA fragment in a given restriction pattern and identification of any particular nucleotide sequence in the mixture (see col. 23, line 1-22). Sorge also explicitly taught tags that are distinguishable by mass spectrometry (see col. 27, line 10-67). An ordinary artisan would have a reasonable expectation of success that inclusion of discrete molecular weight tags that are distinguishable by mass spectrometry would result in enriching sequence information of any oligonucleotide of interest in the mixture and sensitivity of the detectable tags in identifying the sequence information, and such modification of the X-mer mixture would be obvious over the cited prior art in the absence of secondary considerations.

***Response to arguments:***

4. With regard to the rejection made in the previous office action under 35 USC 102(b) as anticipated by Southern et al., Applicants' arguments and amendment are fully considered and found persuasive. The rejection is moot in view of the amendment and new grounds of rejections.

5. With regard to the rejection made in the previous office action under 35 USC 102(b) as anticipated by Brenner, Applicants' arguments and amendment are fully considered and found persuasive. The rejection is moot in view of the amendment and new grounds of rejections.

***Conclusion***

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).




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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Suryaprabha Chunduru  
Examiner  
Art Unit 1637

  
JEFFREY FREDMAN  
PRIMARY EXAMINER  
8/10/05